address metabolic liabilities associated with currently available PET tracers of glutamine metabolism.

Outcomes of Arterial and Caval Resection During Post-Chemotherapy Retroperitoneal Lymph Node Dissection in Metastatic Testicular Cancer

Smith R, Cary C

Background/Objective: In the United States, testicular cancer is the most common solid tumor in men aged 15 to 34. Fortunately, testicular cancer has a cure rate greater than 90% and a 97% five-year survival rate. For the men not cured, a relapse to the retroperitoneum (RP) is most common. Of the patients with RP metastases, a minimal number may require post-chemotherapy retroperitoneal lymph node dissection (PC-RPLND) with resection of the aorta, external iliac, or inferior vena cava (IVC). We hypothesized this procedure would yield reasonable cure rates with acceptable levels of postoperative complications to warrant the indication for surgery.

Methods: Between 2000 and 2020, 2,054 patients with metastatic testicular cancer underwent a PC-RPLND; of those men, 39 also underwent an aortic, external iliac, and/or IVC resection. For the men with a PC-RPLND and vascular resection, demographic, clinical, pathologic, and operative information were reviewed. Next, a Kaplan-Meier curve was created to determine overall survival.

Results: In this retrospective cohort study of 39 patients, PC-RPLND and vascular resection occurred at a median age of 40. The median follow-up of the cohort was 9 months. The median pre-operative mass size was 9 cm and 19 cm in the RP and pelvis, respectively. At PC-RPLND, 54%, 13%, 18%, and 15% of patients demonstrated cancer, teratoma, teratoma and cancer, and necrosis, respectively. Following PC-RPLND and vascular resection, 22 (56%) patients recurred. The median (IQR) time to relapse was 4.2 (2.5 – 8.2) months. Recurrence to the lung was most common, followed by the RP and liver. In total, 17 (44%) patients died of disease with a median overall survival of 14.8 months.

Conclusion: With an overall survival rate of 45% at two years in this heavily pretreated patient population, PC-RPLND with resection of the aorta, external iliac, and/or IVC is reasonable in very select cases.

Targeting Arg-1 and PD-L1 in M2-Tumor Associated Macrophages Impairs Juvenile Myelomonocytic Leukemia (JMML) Cell Proliferation and Migration

Young K, Pasupuleti SK, Stieglitz E, Kapur R

Background and Hypothesis: Tumor-associated macrophages (TAMs) are a key component of tumor-infiltrating immune cells. They are largely characterized into M1 or M2 types. TAMs express an anti-inflammatory M2-like phenotype, promote tumor progression. However, the role of M2-TAMs in driving disease pathogenesis in patients with Juvenile myelomonocytic leukemia (JMML), a rare form of pediatric leukemia driven to a large extent by mutations in the PTPN11 gene, which encodes the phosphatase SHP2 is unclear. We hypothesized that in JMML, inflammatory myeloid cells including neutrophils and M2-TAMs express higher levels of arginase-1 (Arg-1) and PD-L1, which may contribute to the local suppression of immune responses and support the development of JMML.

Methods: To study how alterations in M1/M2 macrophages contribute to JMML development, we utilized a mouse model bearing Shp2E76K mutation (Ptpn11E76K/+) which manifests the cardinal features of human JMML. We hypothesized that Shp2E76K/+ mutations enhance the function of bone marrow derived macrophages (BMDMs), including M2-TAMs and contribute to T-cell suppression.

Results: Our analysis of the bulk RNA-sequence data from 90 JMML patients showed an increase in the expression of Arg-1 and PD-1. Furthermore, single cell RNA-seq analysis of macrophages from 4 JMML patients revealed higher expression of M2-macrophage markers/genes. Our results show that in M2-TAMs, Arg-1 and PD-L1 levels are elevated in BM and spleens of Shp2E76K/+ mice compared to WT. Moreover, M2-TAMs, Arg-1 and PD-L1 levels were also higher in BMDMs derived from Shp2E76K/+ mice compared to WT. The BMDMs from Shp2E76K/+ mice have greater proliferation and migration potential compared to WT BMDMs, which was significantly reduced by inhibiting the function of Arg-1 and PD-L1.

Conclusion: Our results show that M2-TAMs, arginase-1, and PD-L1 create a pro-tumor microenvironment, which likely contributes to the growth of JMML cells. Inhibition of Arg-1 and PD-L1 is a novel therapeutic approach to treat patients with JMML.